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6. The interpretation of the growth of these plants by Mendelian factors is further strongly supported by the distribution of the standard deviations of the plants with different relative sizes. Thus it has been shown that the extreme plants which would be more nearly homozygous and for this reason less variable are, as a matter of fact, some 50 per cent less variable than the plants in the middle class after all allowance has been made for the difference in the size of the means.

This is a preliminary abstract of a paper with the same title now in press in the *Zeitschrift für induktive Abstammungs- und Vererbungslehre.*

ON A NEW GROUP OF BACTERICIDAL SUBSTANCES OBTAINED FROM HEXAMETHYLENETETRAMINE

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Presented to the Academy, February 17, 1915

Ever since the introduction of hexamethylenetetramine into medicine, this drug has attracted wide attention owing to its far-reaching possibilities as an internal antiseptic. In addition to its rapid appearance in the urine it is found after ingestion in practically all the body secretions, including even the cerebrospinal fluid. It is fairly well established that the antiseptic action of the drug is due to the liberation from it of formaldehyde by virtue of the acidity of the medium in which it acts, but that its diffusion throughout the body is a physical property of the undecomposed molecule. In other words, hexamethylenetetramine is but a vehicle for formaldehyde, and if the two conditions are satisfied, firstly, its appearance in large enough amount in the locality desired, and secondly, its cleavage to formaldehyde, a local internal antiseptic action might be expected. Owing, among other things, to the alkalinity of most of the body fluids the limitations set by these prerequisites are obvious.

Numerous attempts have already been made to achieve by proper chemical variation an improvement in the action of the drug. Such attempts, however, which have been confined almost entirely to combinations of hexamethylenetetramine with acids and phenolic compounds, have offered few advantages over the original drug. It seemed to us that more promising results might be obtained by a more direct variation of the hexamethylenetetramine molecule itself and a brief outline of the facts observed in the course of this work is the subject of the following:

The molecule of hexamethylenetetramine functions as a tertiary base, and very readily adds organic substances containing aliphatically bound halogen, forming quaternary salts, a few of which are already described in the literature. In the present work over two hundred such preparations were made, and, after chemical characterization, subjected to biological study.

When tested against various strains of bacteria *in vitro* it was found that with but few exceptions these compounds were bactericidal, the bactericidal power varying with the character of the alkyl or aryl group introduced into the hexamethylenetetramine molecule. These substances are, on the whole, easily soluble in water, but on standing or warming the solutions rapidly decompose, and in the case of the aromatic derivatives, develop a very finely divided emulsion of oil droplets or a colloidal suspension which precipitates more or less readily according to the concentration. On investigation, these decomposition products proved to be the methylene derivatives of the aryl or alkyl amines corresponding to the halides originally used. In the case of the hexamethylenetetramine addition products of the halogenacetylamines these precipitates were more closely studied. In several instances the methyleneglycyl derivatives were isolated in pure crystalline form, and upon testing for bactericidal power, the results were found to agree closely with those obtained with the parent quaternary salts. We are, therefore, led to believe that at least in this type of hexamethylenetetramine derivatives, the bactericidal properties of the parent substances are due to the methyleneglycyl derivatives produced on decomposition, or more particularly, to the methyleneamino group contained in these decomposition products. Since all types of hexamethylenetetramine quaternary salts (with the exception of a few of aliphatic nature) seem to undergo this form of decomposition, we are inclined to believe that in general the methyleneamino compounds are responsible for the bactericidal effect. With the confirmation of this we are at present engaged.

The form in which these methyleneamino compounds separate from the solutions of their parent compounds is a contributing factor in the action of these substances. For when once precipitated from suspension, they cannot readily be redissolved unless they contain a solubilizing group. The use of hexamethylenetetramine in this manner would seem, therefore, but a convenient artifice for obtaining these substances in the form of emulsions or colloidal solutions, conditions necessary for their bactericidal action. In the presence of serum or protein this precipitation is in the majority of cases either diminished or prevented entirely. In this connection it may be stated that with a large number of the compounds the bactericidal effect was found to be but slightly inhibited by serum or protein, a property essential for their use as internal antiseptics. The degree of bactericidal effect obtained depends not only upon the chemical nature of the compound but also upon the organism employed for the test. Comparative experiments with different bacterial species and with different varieties of the same species have demonstrated in many instances remarkable specificity. One class of substances, for example, killed *B. typhosus* in a dilution of 1 to 200 in two hours, whereas, in the same time it killed streptococcus in dilutions of 1 to 50,000 or more. The toxicity of the substances varies naturally with the character of the group added to the hexamethylenetetramine molecule.

A further study of the bactericidal properties of methyleneamino compounds in general is now in progress. A detailed description of the chemical and bacteriological work will follow in the appropriate journals.

CHEMICAL AND PHYSIOLOGICAL STUDIES OF A MAN FASTING THIRTY-ONE DAYS

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Presented to the Academy, March 9, 1915

The important relationship between numerous diseases and the various stages of nutrition and the fact that many pathological cases border on complete or nearly complete inanition make a study of the physiology and chemistry of normal fasting of special importance to the physiologist and the clinician alike. It is rarely practicable to make exhaustive and simultaneous observations in several physiological and chemical fields of study with a subject undergoing a prolonged fast but the arrival in Boston in 1912 of a Maltese, A. Levanzin, who wished particularly to fast thirty-one days under strict scientific observation, presented such an opportunity. It was thus possible to supplement earlier data secured with men during relatively short periods of fasting (2 to 7 days) in the chemical laboratory of Wesleyan University. (Benedict, Carnegie Institution of Washington Publication No. 77, 1907.)

In accordance with a previously arranged program and in coöperation not only with the entire scientific and computing staff of the Nutrition Laboratory but with several members of the faculty of the Harvard Medical School, an extensive study of this man was made. The experiment began April 14, 1912, with a preliminary period of three days with food, followed by thirty-one days of complete abstinence from